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On the effect of sampling rate and experimental noise in the discrimination between microbial growth models in the suboptimal temperature range

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ABSTRACT

Biochemical and microbial processes benefit from mathematical models. Often microbial kinetics are described as a function of environmental conditions in models exploited in predictive microbiology. Based on the organism different model structures are available. However, the aim is to determine the model that describes the system best.

This work deals with secondary models describing microbial kinetics in the suboptimal temperature range and their possibility to be discriminated. The used models are the cardinal temperature model with inflection and its adapted version. The method of Optimal Experiment Design for Model Discrimination is used to investigate the practical (in)feasibility of model discrimination given different noise and sampling frequency values.

Results point out the required steps and the possibilities of the method for model discrimination. It has been observed that discrimination is possible at various noise and sampling frequency levels. Moreover, also the corresponding increase in required experimental effort has been obtained.

1. Introduction

Mathematical models are important tools for the analysis, monitoring, control and optimization of biochemical and microbial processes. Also for describing microbial processes in food and food processing mathematical models have been constructed (see, e.g., Saravacos and Kostaropoulos, 1996; Blau et al., 2008). These models have been typically used in view of product safety, product stabilization and process design and operation and are nowadays also extended towards food design (Trystram, 2012).

Microbial kinetics play a key role in these models as these kinetics determine the dynamic microbial evolution in time. The domain of *predictive microbiology* deals with mathematical models for describing this microbial kinetics as a function of environmental conditions. Depending on the micro-organism and the application, different models are used for describing microbial growth, survival and/or inactivation in food products under possibly time varying environmental conditions. The environmental conditions can include, e.g., temperature, pH or background flora. A two step modelling approach is classically used in predictive microbiology. The first step consists of a *primary model*. This model describes the evolution of microbial concentration with time, under constant environmental conditions. In the second step, the parameters of the primary model are described by a *secondary model* as a function of changing environmental conditions (Baranyi and Roberts, 2004). When combining both primary and secondary models, microbial behavior can be described in a dynamic environment.

However, challenges when modeling microbial processes typically involve (i) the difficulty for performing experiments and obtaining numerous reliable data, (ii) the uncertainties on measurements and experimental data and (iii) the uncertainties concerning food properties (Trystram, 2012). Nevertheless, despite these challenges models which have a significant predictive power are desired. In this respect, first an appropriate kinetic model structure has to be found. In chemical engineering literature, this question has been widely studied and strategies for optimal design of (dynamic) experiments in view of model discrimination, i.e., *optimal experiment design for model discrimination* (OED/MD), have been reported, e.g., Burke et al. (1994), Buzzi Ferraris et al. (1984), Buzzi-Ferraris et al. (1990), Ungarala and Co (2000), Asprey and Macchietto (2000), Chen and Asprey (2003a), Schwaab et al. (2008), Donckels et al. (2009), Donckels et al. (2010), Luo et al. (2015).

There exist several criteria for discrimination. One of the first simple criteria has been developed by Hunter and Reiner (1965). For

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discriminating between two rival models, the new experimental condition should give model responses with the maximum difference. Since the first proposal, other criteria have been developed, with the criterion of Buzzi-Ferraris and Forzatti (1983) introducing the model deviations variance in the criterion. One of the latest extensions is the criterion proposed by Schwaab et al. (2008) and in parallel by Donckels et al. (2009). In this technique, the posterior covariance matrix of the difference between model predictions is taken into account during the design. Through this approach, apart from discrimination, also improved parameter estimates are achieved.

The aim of the current paper is evaluate the influence of practical limitations (e.g., limited sampling rate and inherent experimental noise) on the (im)possibility to discriminate between microbial kinetic models for growth in the suboptimal temperature range. This suboptimal temperature range (i.e., below the temperature at which growth is at its maximum) is of high importance for practical applications as this is typically the temperature range in which food products are stored and transported. However, it is also a difficult temperature range to model as growth is typically slow, microbial concentrations are low and the experimental noise is high (compared to the low microbial concentration values).

Two well-known secondary models for microbial kinetics are selected. These models describe the influence of temperature on microbial growth: the cardinal temperature model with inflection (CTMI) (Rosso et al., 1993) and its adapted version (aCTMI). Up until now, exceptions have been reported only for *Listeria monocytogenes* (Bajard et al., 1996) and *Listeria innocua* (Le Marc et al., 2002). The difference for *Listeria* is in the suboptimal temperature region, where the plot of the square root of the maximum growth rate (μ_{max}) as a function of temperature, displays two linear phases. Listeria is the mircoorganism causing infections mainly to the central nervous system, i.e. listeriosis (Baron, 1996). The growth monitoring in the suboptimal temperature range is important for chilled, prepared food products (Le Marc et al., 2002).

The paper is divided as follows. In Section 2 the mathematical models for describing the suboptimal temperature range are presented. Following in Section 3 the procedure for optimal experiment design for model discrimination is explained. Whereas in Section 4 the practical implementation is outlined. The results found are described and discussed in Section 5 and finally the main conclusions are summarized in Section 6.

2. Mathematical models for describing the suboptimal temperature range

As mentioned in Section 1, combining a primary with a secondary model allows to describe the microbial behavior in a dynamic environment.

The primary model used is the one proposed by Baranyi and Roberts (1994). The cell density is described as a function of time as seen below:

$$\begin{aligned} \frac{dn(t)}{dt} &= \frac{Q(t)}{Q(t)+1}\cdot\mu_{\max}(T(t))\cdot[1-\exp(n(t)-n_{\max})] \\ \frac{dQ(t)}{dt} &= \mu_{\max}(T(t))\cdot Q(t) \\ n(0) &= n_0 \\ Q(0) &= Q_0 \end{aligned} \tag{1}$$

with $n(t)$ [ln(CFU/mL)] the cell density at time t [h], n_{max} [ln(CFU/mL)] the maximum value for $n(t)$ and μ_{max} [1/h] the maximum specific growth rate. $Q(t)$ is a measure for a physiological state of the cells. The initial values for $n(t)$ and $Q(t)$ for time $t=0$ are n_0 and Q_0, respectively. In this work, $Q(t)$ is excluded, in other words it is assumed that there is no lag phase (see Van Derlinden et al. (2010) for details), and thus the model is reduced to:

$$\frac{dn(t)}{dt} = \mu_{\max}(T(t))\cdot[1-\exp(n(t)-n_{\max})] \tag{2}$$

The microbial growth rate as a function of temperature (secondary model) can be described by the CTMI (Rosso et al., 1993) and the aCTMI (Le Marc et al., 2002). For simplicity the temperature evolution $T(t)$ will be noted as T in the following.

The CTMI is described by:

$$\mu_{\max}(T) = \gamma(T)\cdot\mu_{opt} \tag{3}$$

with:

$$\gamma(T) = \begin{cases} 0 & T \le T_{\min} \text{or} T \ge T_{\max} \\ \dfrac{(T-T_{\min})^2(T-T_{\max})}{(T_{opt}-T_{\min})((T_{opt}-T_{\min})(T-T_{opt})-(T_{opt}-T_{\max})(T_{opt}+T_{\min}-2T))} & T_{\min} < T < T_{\max} \end{cases} \tag{4}$$

The parameters included in this model are the three cardinal temperatures T_{min} [°C], T_{opt} [°C] and T_{max} [°C] (i.e., the minimum, optimum and maximum temperature for growth, respectively) and μ_{opt}[1/h] (the maximum specific growth rate at T_{opt}).

The aCTMI is described in a similar way as the CTMI but with a different $\gamma(T)$ function:

$$\gamma(T) = \begin{cases} 0 & T \le T_{\min} \text{or} T \ge T_{\max} \\ \dfrac{(T_c-T_1)^2(T_c-T_{\max})}{(T_{opt}-T_1)((T_{opt}-T_1)(T_c-T_{opt})-(T_{opt}-T_{\max})(T_{opt}+T_1-2T_c))}\left(\dfrac{T-T_{\min}}{T_c-T_{\min}}\right)^2 & T_{\min} < T \le Tc \\ \dfrac{(T-T_1)^2(T-T_{\max})}{(T_{opt}-T_1)((T_{opt}-T_1)(T-T_{opt})-(T_{opt}-T_{\max})(T_{opt}+T_1-2T))} & T_c < T < T_{\max} \end{cases} \tag{5}$$

Apart from the previous four parameters the adapted model is defined also by T_c [°C], the so-called change temperature, and T_1 [°C], the intersection point between the first linear part and the temperature axis. In Fig. 1, the square root of the maximum growth rate as a function of temperature is displayed for the two models, and their difference in the region of T_{min} can be seen.

3. Procedure for optimal experiment design for model discrimination

When having to choose among two (or more) models, optimal experiment design for model discrimination is a reliable tool (see modeling cycle (Ljung, 1999)). In this section, the technique proposed by Schwaab et al. (2008) and Donckels et al. (2009), will be highlighted.